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Stefan Muhlbauer

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EXAMINER

KUBELIK, ANNE R

ART UNIT

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/581,703	Applicant(s) MUHLBAUER, STEFAN	
	Examiner Anne R. Kubelik	Art Unit 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 October 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,26-28,36 and 41-47 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,26-28,36 and 41-47 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Claims 1, 26-28, 36 and 41-47 are pending.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
3. The rejection of claims 1-2, 6, 20, 22-28 and 30-42 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in light of Applicant's cancellation of claims.
4. The rejection of claims 6, 9 and 16 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention is withdrawn in light of Applicant's cancellation of the claims.
5. The rejection of claims 1-2, 6, 9-13, 15-18, 26, 30, 32-34 and 36-37 under 35 U.S.C. 102(b) as being anticipated by McBride et al (1999, US Patent 5,925,806) is withdrawn in light of Applicant's cancellation or amendment of the claims.
6. The rejection of claims 1-6, 9-11, 19-26, 28, 30-31, 33-39 and 41-42 under 35 U.S.C. 103(a) as being unpatentable over McBride et al (WO 01/02593) in view of Sues et al (2004, Nuc. Acids Res. 32:1610-1614) is withdrawn in light of Applicant's cancellation or amendment of the claims.
7. The rejection of claims 1-2, 6, 9-18, 26, 30, 32-34 and 36-37 under 35 U.S.C. 103(a) as being unpatentable over McBride et al (1999, US Patent 5,925,806) is withdrawn in light of Applicant's cancellation or amendment of the claims.

Claim Rejections - 35 USC § 103

8. Claims 1, 26-28, 36, and 41-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over McBride et al (WO 01/02593 in view of Maliga (1996, US Patent 5,530,191). Because of applicant's amendment of the claims, the rejection is modified from the rejection set forth in the Office action mailed 14 April 2008, as applied to claims 1-11, 17-19, 26-28, 30-31, and 33-42. Applicant's arguments filed 13 October 2008 have been fully considered but they are not persuasive.

The claims are drawn to a method of controlling the expression of a plastome-encoded sequence of interest in a plant by externally applying to a plant a chemical signal that controls expression of the sequence of interest via the lac operators/repressors.

McBride et al teach a method comprising exposing, by direct application, a plant to a chemical activating compound, acetylated homoserine lactone (AHL), wherein the chloroplasts of said plants are transformed with a construct comprising the GUS coding sequence (the sequence of interest) expressed under control of the luxI promoter/operator and the luxR protein (pg 43, paragraph 3, to pg 45, paragraph 1; pg 50, paragraphs 1-4; claims 17-22; Fig. 19-23). The luxI promoter is an AHL-response element, and AHL is a nonproteinoaceous chemical signal. In this arrangement, AHL activated the luxR protein, changing its binding affinity to luxI, activating expression of GUS; the luxR protein is not involved in expression of other plastid sequences. The regulatory protein also encoded on the construct (Fig 19-22). LuxR is of prokaryotic origin.

McBride et al do not teach use of the lac operator and repressor.

Maliga teaches a method controlling expression of plastome-encoded sequence of interest, wherein plants, whose nuclei are transformed with construct comprising a nuclear promoter operably linked to a sequence encoding a plastid transit peptide operably linked to a regulator polypeptide, and whose plastids are transformed with a construct comprising a male-sterility gene (the sequence of interest) under control of the regulator polypeptide (claims 1, 3-7). The regulator polypeptide includes the T7 polymerase (claim 10). The plastid construct can comprise a target sequence for preventing gene expression, regulated by, for example, the lac repressor (claims 16, 27, 31)

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of controlling the expression of a plastome-encoded sequence of interest in a plant by externally applying to a plant a chemical signal that controls expression of the sequence of interest as taught by McBride et al, to substitute the lac operators/repressors described in Maliga for the luxI promoter/operator. One of ordinary skill in the art would have been motivated to do so because substitution of one type of operator system for another is an obvious design choice. Further, McBride et al teaches that the tetR system is analogous to the luxR system (pg 18, paragraph 2). One of ordinary skill in the art would have substituted IPTG for AHL because this is the chemical controls for the lac operator/repressors.

Applicant urges that McBride relates to controlling nuclear and plastid gene expression using the AHL quorum system, and has little disclosure of controlling plastid gene expression, including no example demonstrating functionality in plastids, including externally applying a chemical control signal to a plant. The work on pg 50 does not indicate what the plastids were transformed with; McBride can at best be considered a suggestion (response pg 11-12).

This is not found persuasive. Applicant has not indicated what, if any, of McBride et al would not work. Pg 50, paragraph 3, indicates that AHL was applied to the plants.

Applicant urges that Maliga does not relate to controlling expression of a plastid encoded sequence by externally applying a chemical control signal to a plant, and no lactose or lactose analog is used (response pg 12-13).

This is not found persuasive. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicant urges that neither McBride nor Maliga suggest that lactose or an analog thereof can be used to control expression of a plastid encoded sequence, or that it would cross the two plastid membranes (response pg 13).

This is not found persuasive. Substitution of one operator/repressor system for an even more well-known one is obvious, and in the case of the lac repressor system has the advantage of having more readily available components. Applicant has not indicated why one of skill in the art would think that lactose could not cross the two plastid membranes, given the large number of complex molecules that do so cross, like those used in selection methods, as well as other sugar molecules. See for example, US 5,877,402, cited in Applicant's IDS, in which spectinomycin (example 1), kanamycin, (example 3), and the beta-glucuridase substrates X-glu, MU and and MUG (example 4) were all shown to cross the plastids membranes.

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Applicant urges that the combination of the lac repressor with externally applied lactose or an analog thereof is excluded by the presence of lactose preventing the repressive effect of the lac repressor (response pg 13).

This is not found persuasive because one of skill in the art understands how the lac operator/repressor system works, and could adapt the system to function

Applicant urges that no suggestion can be derived from the cited portion of McBride that the tet system can be used for controlling expression of the plastid encoded sequence, or that tetracycline could cross the two plastid membranes, or that the tet two factor system is analogous to that of lac (response pg 13-14).

This is not found persuasive because Applicant has not indicated why one of skill in the art would think that these systems would not work or that tetracycline or lactose could not cross the two plastid membranes. McBride suggests using other operator/repressor systems. As skilled artisans would understand how well-known systems such a tet and lac work, they could design the system to take advantage of the strengths and features of a given operator/repressor system.

Applicant urges that one of skill in the art would not have combined McBride and Maliga, or if they had, would not have all the elements of the claimed invention (response pg 14).

This is not found persuasive because Applicant has not indicates what elements are missing, or why one of skill in the art would not have combined McBride and Maliga.

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Conclusion

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, Ph.D., whose telephone number is (571) 272-0801. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg, can be reached at (571) 272-0975.

The central fax number for official correspondence is (571) 273-8300.

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

January 14, 2009

/Anne R. Kubelik/

Primary Examiner, Art Unit 1638